

Inventing the Future

Dr. Lee Hood, President and Co-Founder of ISB

ISB was founded in 2000 to invent the future as the first institute to pioneer systems science and its applications to biology and disease. ISB has made remarkable progress in its first 13 years.

We have pioneered the emergence of systems biology as a field, developing new strategies and applying them to fundamental problems in biology and medicine.

We have developed powerful new technologies (e.g. proteomics and genomics) and have pioneered a vast array of analytical tools for the life sciences.

We have applied systems thinking to the study of disease and catalyzed the development of a systems medicine that has already reached a tipping point and is changing the practice of healthcare, improving it, beginning to reduce its costs, and promoting innovation and the creation of new companies. The convergence of three major thrusts in healthcare—systems medicine, big data analysis and patient-activated social networks—has led to the emergence of a medicine that is **predictive, preventive, personalized and participatory (P4 medicine)** with the two major objectives of quantifying wellness and demystifying disease. P4 medicine will thus catalyze an ability to predict and prevent disease before it happens, empowering individuals with self-knowledge and catalyzing new dimensions of wellness. My own belief is that in the next 10 to 15 years, the wellness industry will grow to far exceed the healthcare industry.

The **metrics for our success** are many and are exemplified by two recent reports: The National Academy of Science published a report in 2009 on the "New Biology" that described systems biology perfectly and asserted it was the future for solving the fundamental problems of the life sciences—biology, healthcare, environment, agriculture, etc. The Spanish SCImago Institute has ranked almost 3,300 research institutions for the impact of their papers in all areas of science and ISB ranked fourth in the world in excellence of its papers. ISB's papers cover biology, medicine, technology and computation/mathematics, reflecting the cross-disciplinary culture that lies at the heart of our success.

ISB invented the field of systems biology over the past decade. **But how can we foster a new vision that will let us invent a transformational future?** Although we are still debating this question, I want to discuss with you one proposal that fascinates me: pioneering the field of wellness.

I would like to propose that ISB catalyze a longitudinal study of 100,000 "well" individuals over 25 years, creating for each a virtual cloud of billions of data points that include (1) their genome sequences to identify actionable gene variants for which suggestions can be made for improving health; (2) longitudinal blood measurements two to three times a year for analysis with traditional clinical chemistries and assays that employ systems strategies (see below); and (3) high-frequency digital measurements coming from "quantified self" assessments that track exercise, sleep, stress, weight and nutrition.

The systems-driven assays that would enable us to track transitions from wellness to disease would include: (1) analyses of 10 or more organ-specific blood fingerprints that will allow us to track wellness in major organs including the brain, heart, liver, lung, etc.; (2) omics-characterizations of white blood cells to track inflammation and immune responses in each individual; (3) protein chips with 10,000 human proteins to identify autoantibodies (characteristic of autoimmune diseases such as rheumatoid arthritis and perhaps other diseases such as cancers and neurodegenerative diseases); and (4) track the human gut microbiome through stool analyses (which correlates in many different ways with wellness and susceptibility to diseases such as diabetes and heart disease).

These 100,000 virtual data clouds for individuals will **provide invaluable data for optimizing wellness** for each individual and they will permit us to identify effective metrics for assessing wellness of each individual, as well as markedly cut his or her costs for healthcare. In addition, we will see among these 100,000 patients transitions from wellness into major diseases. This will provide an early molecular warning for each of these diseases that will permit many to be managed more effectively. In the long run, we will accumulate massive amounts of information from these virtual data clouds that can be mined for the predictive medicine of the future. This effort would require the recruitment of patients from medical centers and community hospitals in the Seattle area, as well as research and academic centers to help develop the strategies, technologies and analytical tools necessary to generate and analyze these data. In the longer run, this database could provide information for spinning off diverse wellness and healthcare companies. This is a vision that could transform two massive industries and, indeed, make Seattle the Silicon Valley of the wellness market. ISB is in a unique position to initiate

such an effort, because it has been pioneering P4 medicine, with a focus on wellness; it has developed a variety of technologies that will contribute to diagnostic assays that will reveal new dimensions of patient data space; and it has strong computation and mathematical skills for acquiring, storing, mining, integrating and creating predictive and actionable models from each of the 100,000 virtual data clouds. It would be an exciting challenge for the scientists in all our labs to **invent this future, utilizing powerful systems biology and systems medicine approaches** to explore new dimensions of patient data space and develop new analytical tools to integrate and model the data.

In addition to the technical challenges, there would be striking societal challenges that could be the domain of the P4 Medicine Institute, a nonprofit institute dedicated to the fourth P—participatory—in P4 medicine. A key challenge is to develop a value proposition for healthcare consumers that would (1) engage them in using the actionable personalized health information which systems medicine can provide and (2) incentivize them to collect data that can be made available to mine for the predictive medicine of the future that will revolutionize healthcare for our children and grandchildren. Major questions would include how we can capture data in a way that is seamlessly incorporated in people's daily lives; how to properly de-identify the data and protect people from abuses—which will involve additional legislation and regulatory action.

There are also striking challenges as to how we will educate patients, physicians, the healthcare community, payers and providers, and federal and state policy makers about the nature of this medicine. The solution will undoubtedly require the use of large-scale information technology. We will have to create a new profession of coaches who can bring insights gained from mining individual data clouds to individual patients. Finally, there is the challenge of funding this effort and identifying the types of organizations that should participate in this incredibly ambitious—and transformative—future.

There is no doubt in my mind this vision would **further catalyze the profound paradigm change in healthcare** that P4 medicine entails. This is a most ambitious new vision that would enable ISB to continue to invent the future through systems thinking around the strategies, technologies and analytics tools of P4 medicine and wellness. 🌱

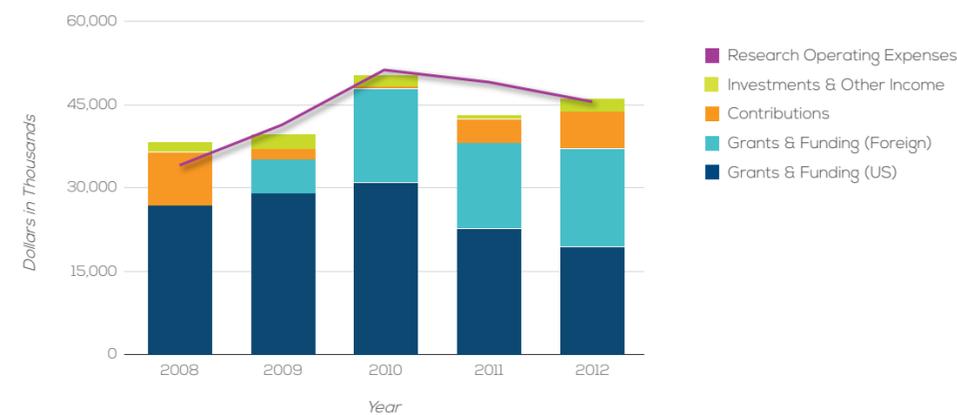
Financial Statement

Year Ending December 31, 2012

While the full impact of sequestration has yet to be seen, there's no doubt that all nonprofit organizations are experiencing the challenges of facing reduced funding. ISB was able to increase total revenue in 2012, which is bright news in this difficult financial time. We have been diligent about cultivating our funding and contributor networks to ensure ISB can continue to achieve breakthroughs in deciphering some of the most complex diseases that affect our lives. We also have done the hard work of further streamlining our research operating expenses to help create a sustainable financial future.

5-Year Growth Comparison

Research Operating Expenses vs. Total Revenue



Balance Sheet

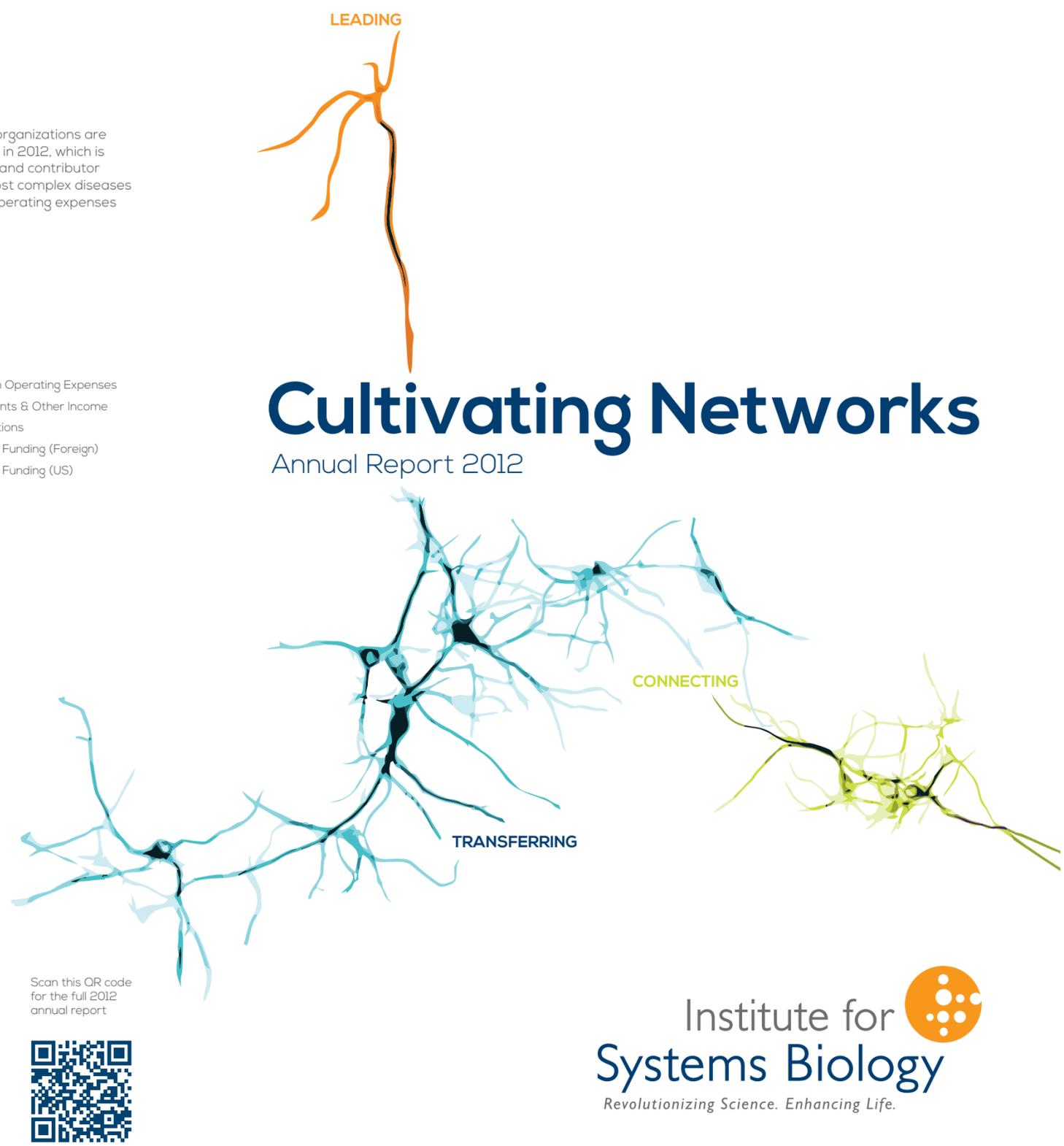
Dollars in Thousands

Assets	\$
Cash & Investments	18,183
Other Assets	10,007
Property & Equipment (Net)	15,327
Total Assets	43,517
Liabilities	\$
Accounts Payable & Accrued Expenses	18,710
Deferred Revenues	4,287
Notes Payable	8,344
Total Liabilities	31,341
Net Assets	\$
Unrestricted Net Assets	(308)
Temporarily Restricted Net Assets	3,812
Permanently Restricted Net Assets	8,672
Total Net Assets	12,176

Statement of Activities

Dollars in Thousands

Revenues	\$	%
Grants & Contract Revenue	37,018	80.1
Contributions	6,737	14.6
Investments & Other Income	2,480	5.4
Total Revenues	46,235	100.0
Expenditures	\$	
Research & Other Direct Costs	34,213	
Management & General	11,163	
Fundraising & Other	186	
Total Expenditures	45,562	
Increase in Net Assets	673	



Scan this QR code for the full 2012 annual report

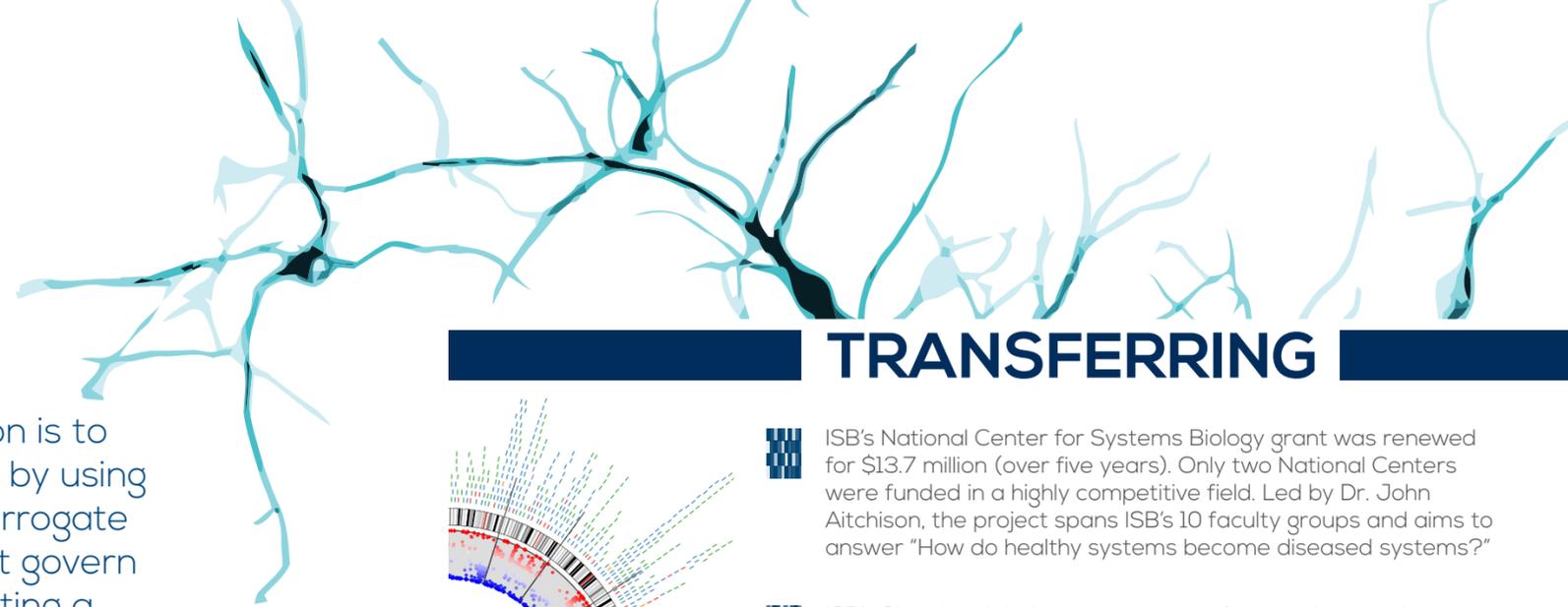


Institute for
Systems Biology
Revolutionizing Science. Enhancing Life.

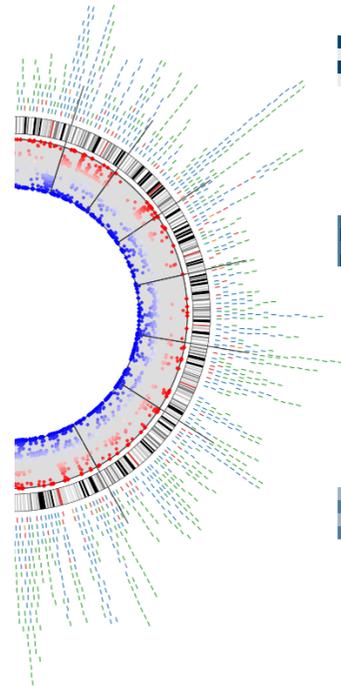
Cultivating Networks

Institute for Systems Biology's mission is to revolutionize science and healthcare by using the power of systems biology to interrogate the complex molecular networks that govern wellness and disease. We are cultivating a global understanding and practice of the systems approach, which we pioneered and for which we serve as its most committed advocate. Here, we highlight nine headlines from 2012.

For ISB's full 2012 annual report, please visit: annualreport.systemsbiology.net



TRANSFERRING



■ ISB's National Center for Systems Biology grant was renewed for \$13.7 million (over five years). Only two National Centers were funded in a highly competitive field. Led by Dr. John Aitchison, the project spans ISB's 10 faculty groups and aims to answer "How do healthy systems become diseased systems?"

■ ISB's Shmulevich Lab serves as one of seven data analysis centers participating in The Cancer Genome Atlas (TCGA) and co-authored the paper "Comprehensive molecular characterization of human colon and rectal cancer" that was published in *Nature*. ISB's unique contribution was the creation of the Cancer Regulome Explorer web tool that allows researchers to explore the molecular signatures of cancers, including aggressive colorectal cancer (pictured left).

■ There are 10 times the number of microbes than human cells on and in your body. How do the good and bad bacteria interact and coexist? ISB's 11th Annual Symposium: Systems Biology and the Microbiome explored this question and showcased presentations from leading researchers - including keynote speaker Dr. Craig Venter - from across the country.

CONNECTING



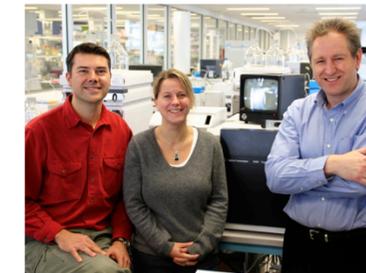
■ ISB and Sapphire Energy announced a strategic partnership to research commercial algae production for fuel. Dr. Nitin Baliga, ISB's Director, leads the project, which is applying systems biology to find the mechanisms in algae that can increase yield in order to scale fuel production. (Photo © Sapphire Energy)

■ As part of a strategic partnership with the Grand Duchy of Luxembourg, ISB continued its collaboration with the Luxembourg Centre for Systems Biomedicine (LCSB) on research related to cancers, Parkinson's disease and the human microbiome.

■ ISB's Shmulevich Lab was featured in the keynote presentation at Google I/O developers conference. The segment showed off our Cancer Regulome Explorer web tool, using Google App Engine and Compute Engine. This showcased ISB's technology on a world stage.

LEADING

Targeted Proteomics Named 'Method of the Year'



■ ISB has been on the forefront of proteomics since its founding in 2000. While DNA as the blueprint of life is important to understand, it's the proteins that comprise the tiny molecular machines doing the actual work of growing cells and controlling functions or causing dysfunctions. In December 2012, *Nature Methods* chose targeted proteomics as the "Method of the Year" and featured ISB's Moritz Group among the leading researchers who are pioneering the technique. (Pictured from left to right: Dr. Eric Deutsch, Dr. Ulrike Kusebauch and Dr. Robert Moritz.)

Dr. Lee Hood Receives National Medal of Science

■ On Dec. 21, 2012, the White House announced that Dr. Lee Hood, ISB's President and Co-Founder, had been named a recipient of the 2011 National Medal of Science. This is the highest honor the U.S. President can bestow upon scientists. "This is exciting because it's for lifetime achievement," Lee commented, "which lauds all my colleagues." (Lee would travel to the White House in February 2013 for the medal ceremony, pictured right.)



ISB Celebrates Its History as Champions of Quality K-12 Science Education



■ One of ISB's core beliefs is the importance of being fully engaged in how science is taught and learned at all levels - especially grades K-12. On Nov. 29, 2012, ISB held its first annual Valerie Logan Luncheon to honor Valerie Logan, Dr. Lee Hood's wife, and to raise funds for our education work. Valerie was instrumental in helping to establish ISB as a leader in advocating and implementing systems education. The luncheon raised about \$64,000 to support ISB's groundbreaking K-12 programs for educators and students. (Photo: Valerie Logan celebrates with her family.)